

REMARKS

By the present Amendment, Claims 1, 3, 4, 14, 16, and 17 are pending. Claims 2, 5, 6, 10-13, 15, 18-23 have been cancelled. Claims 7-9 remain cancelled. Claims 1, 3, 4, 14, 16, and 17 are amended. Claims are amended or cancelled without prejudice to, or disclaimer of, the underlying subject matter. Support for the present amendments may be found throughout the specification and in the original claims as filed. No new matter enters by these amendments.

I. 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1, 2, 5, 6, 10-15, and 18-23 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner alleged that “[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention” Final Action at page 2. Though Applicants disagree, to facilitate prosecution, claims 1, 2, 5, 6, 10-15, and 18-23 have been amended or cancelled without prejudice to, or disclaimer of, the underlying subject matter. Applicants believe that upon entry of the claim amendments, the written description rejection is rendered moot and request its withdrawal.

II. 35 U.S.C. § 102(b)

Claims 1-3, 5-6, 10-16, and 18-23 were rejected under 35 U.S.C. 102(b) as being anticipated by Tracey *et al* (hereinafter “Tracey”). *Id.* at page 5. Applicants respectfully traverse this rejection.

In order for a claim to be anticipated, a reference must teach every element of the claim. M.P.E.P. § 2131. That is, “a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, (Fed. Cir. 1987).

At best, Tracey teaches “methods of reducing tissue damage resulting from ischemia which comprise administering . . . a combination . . . of an NHE-1 inhibitor and a second compound”. See *e.g.*, Tracey at abstract (emphasis added). In Tracey, the second compound is at best selected from five generic classes of compounds, including “(a) a complement modulator, (b) a metabolic modulator, (c) an anti-apoptotic agent, (d) a nitric oxide synthase-related agent, and (e) an enzyme/protein modulator.” See *e.g.*, Tracey at abstract. As acknowledged by the Examiner, “Tracey *et al* do not mention use of the AMPK inhibitors, compound C or C75.” Final Action at page 6.

Whatever else Tracey teaches, Tracey does not teach a “method of neuroprotection in a subject who is experiencing or has experienced a stroke, or other interruption of cerebral blood flow by other etiologies, the method comprising: administering a neuroprotective amount of a compound to a subject in need thereof, wherein said compound is C75 or Compound C,” let alone a “method of neuroprotection in a subject who is experiencing or has experienced a stroke, or other interruption of cerebral blood flow by other etiologies, the method consisting essentially of: administering a neuroprotective amount of a compound to a subject in need thereof, wherein said compound is C75 or Compound C.” See *e.g.*, Claims 1 and 14.

As such, Applicants respectfully submit that upon entry of the claim amendments, the anticipation rejection is rendered moot and request its withdrawal.

III. 35 U.S.C. § 103(a)

Claims 1-3, 5-6 and 10-16, and 18-23 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tracey in view of Kim *et al* (hereinafter “Kim”). Further, claims 1, 2, 4-6 and 10-15, and 17-23 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tracey in view of Leon *et al* (hereinafter “Leon”). In making the rejections, the Examiner asserted that “[i]t would have been obvious to one of ordinary skill in the art at the time of filing Applicants’ invention to use the AMPK inhibitor of Kim in Tracey’s method of treating ischemia with AMPK inhibitors with a reasonable expectation of success.” Final Action at page 6. Similarly, the Examiner asserted that “[i]t would have been obvious to one of ordinary skill in

the art at the time of filing Applicants' invention to use the AMPK inhibitor of Leon in Tracey's method of treating ischemia with AMPK inhibitors with a reasonable expectation of success" *Id.* at page 7. Applicants respectfully disagree.

The Office has not met the basic criteria to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of skill in the art, to modify the reference or to combine reference teachings. There must also be a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Moreover, "[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning **with some rational underpinning** to support the legal conclusion of obviousness." *KSR Int'l. Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1741 (2007) quoting *In re Kahn* 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added). "Obviousness requires more than a mere showing that the prior art includes separate references covering each separate limitation in a claim under examination." *Id.* at 418. "Rather, obviousness requires the additional showing that a person of ordinary skill at the time of the invention would have selected and combined those prior art elements in the normal course of research and development to yield the claimed invention." *Id.* at 421.

Initially, the claims under consideration are directed to methods of neuroprotection which comprise administering compound C or C75 to a subject who is experiencing or has experienced a stroke, or other interruption of cerebral blood flow by other etiologies and is in need of neuroprotection. Whatever else Tracey may disclose, it does not teach or suggest the use of compound C or C75 for neuroprotection. The Examiner also acknowledged that "Tracey et al do not mention use of the AMPK inhibitors, compound C or C75." Final Action at page 6.

As set forth above, Tracey at best teaches "methods of reducing tissue damage resulting from ischemia which comprise administering . . . a combination . . . of an NHE-1 inhibitor and a second compound". See e.g., Tracey at abstract (emphasis added). In Tracey, the second compound is at best selected from five generic classes of compounds, including "(a) a

complement modulator, (b) a metabolic modulator, (c) an anti-apoptotic agent, (d) a nitric oxide synthase-related agent, and (e) an enzyme/protein modulator.” *See e.g.*, Tracey at abstract. Tracey then continues, suggesting that the disclosed method may be useful in reducing brain tissue damage resulting from ischemia. *See, e.g.*, Tracey at claims 15 and 16. However, nowhere is it even suggested by Tracey that this long listing of second compounds **itself** might be effective to reduce brain tissue damage, let alone neuroprotective.

In fact, in light of the Hardie article (hereinafter “Hardie”), submitted by Applicants’ May 5, 2011 Information Disclosure Statement, one of ordinary skill in the art would have no reason to believe that AMPK inhibition is in any way neuroprotective. Indeed, to the contrary, Hardie refers to a study by Kuramoto, suggesting that “AMPK activation is neuroprotective” *See e.g.*, Hardie at abstract.

In this regard, the present claims require a method of neuroprotection which comprise administering compound C or C75 to a subject who is experiencing or has experienced a stroke, or other interruption of cerebral blood flow by other etiologies and is in need of neuroprotection. The Federal Circuit has directly addressed this issue of claim interpretation, and held that “the claims’ recitation of a patient or a human ‘in need’ gives life and meaning to the preambles’ statement of purpose. [. . .] The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed.” *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003) (*citations omitted*).

In *Jansen*, the Federal Circuit interpreted a claim directed to a “method of treating macrocytic-megaloblastic anemia in . . . a human in need thereof,” and held that the claim preamble is a limiting “statement of intentional purpose.” *Id.* The Court explained that “administering the claimed vitamins in the claimed doses for some purpose other than treating or preventing macrocytic-megaloblastic anemia is not practicing the claimed method.” “[T]he combination of folic acid and vitamin B[12] must be administered to a human with a recognized need to treat or prevent macrocytic-megaloblastic anemia.” *Id.* at 1334.

In accordance with proper claim interpretation, the present claims require a method comprising the administration of compound C or C75 in an amount effective and for the intended purpose of neuroprotection in a patient with a recognized need for such neuroprotection. The mere disclosure in Tracey of a combination treatment involving the administration of a combination of an NHE-1 inhibitor and a second compound does not amount to a teaching or suggestion of the claimed subject matter.

As mentioned above, nothing in Tracey, Kim, nor Leon teaches or suggests a method with an intent of neuroprotection, by administering compound C or C75 to a subject who is experiencing or has experienced a stroke, or other interruption of cerebral blood flow by other etiologies and is in need of neuroprotection. Absent a suggestion of such a method, one of skill in the art would simply find no motivation to perform a method as recited in the present claims for the specific intended purpose. Further, there is no motivation to specifically modify the teaching of Tracey so as to arrive at the specifically claimed methods with any reasonable expectation of success. In fact, Hadie teaches away from achieving neuroprotection by inhibiting AMPK. For at least these reasons, one of ordinary skill in the art would not look to modify the teachings of Tracey alone or in view of Kim or Leon so as to arrive at the claimed subject matter.

In addition, Applicants note that claim 14 and its dependent claims recite a method “consisting essentially of” administering a neuroprotective amount of compound C75 or Compound C to a subject in need thereof. Whatever else the cited references disclose, there is no teaching or suggestion of administration of the recited compounds in the absence of combination therapy for neuroprotection, much less administration in a neuroprotective amount.

As such, withdrawal of the obviousness rejections is therefore respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the present application is in condition for allowance and respectfully request notice of such. The Examiner is encouraged to contact the undersigned at 202-942-6195 if any additional information is necessary for allowance.

Respectfully submitted,



Milan M. Vinnola (Reg. Atty. No. 45,979)
Xianfeng Xu (Reg. Agent No. 68,376)

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ARNOLD & PORTER LLP
Attn: IP Docketing
555 Twelfth Street, N.W.
Washington, D.C. 20004-1206
(202) 942-5000 telephone
(202) 942-5999 facsimile